

**In the Claims:**

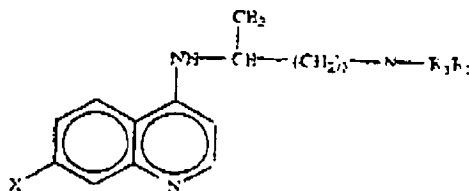
Claim1. (presently amended) A complex comprised of at least one negatively charged nucleic acid and at least one positively charged polymeric conjugate with the bond therebetween being electrostatic in nature, the polymeric conjugate containing a polylysine formed from monomers having free  $\text{NH}_3^+$  groups.

at least 10% of free  $\text{NH}_3^+$  groups of the said polylysine are substituted by residues which are protonated in a weakly acid medium causing destabilization of cell membranes,

and optionally at least one free  $\text{NH}_3^+$  group of the said polylysine is substituted by a molecule with a recognition signal recognized by a cell membrane receptor,

with the proviso that all the free  $\text{NH}_3^+$  groups of the said polylysine make up at

least 30% of the number of monomers of the skeleton of the polymeric conjugate wherein said residues causing destabilization of cell membrane in a weakly acid medium are selected from the group consisting of family of compounds having an imidazole nucleus, pterines, pyridines and quinolines of the formula:



in which  $R_1$  is hydrogen,  $R_2$  is  $-(CH_2)_n-CO_2-H$ ,  $X$  is hydrogen or chlorine and  $n$  is an integer from 1 to 10, wherein said recognition signal is selected from the group consisting of:

- a) simple osides selected from the group consisting of  $\alpha$  or  $\beta$  conformers of 2-deoxy, 2-amino or 2-deoxy, 2-acetamide neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of glycuronic acid derivatives of neutral monosaccharides,  $\alpha$  or  $\beta$  conformers of L-iduronic acid, of keto-deoxy-octonic acid, of N-acetyl neuraminic acid or of N-glycoloyl-neuraminic acid; and  $\alpha$  or  $\beta$  conformers of neutral 6-deoxy monosaccharides;
- b) a disaccharide selected from the group consisting of lactose and mannopyranosyl  $\alpha$ -6-mannopyranose,
- c) complex osides selected from the group consisting of Lewis<sup>a</sup>, Lewis<sup>b</sup>, Lewis<sup>x</sup>, oligomannosides and oligolactisoamines and
- d) peptides.

Claim 2. (previously presented) The complex of claim 1 wherein said quinolines are selected from the group consisting of 7-chloro-4-(amino-1-methyl-butylamino)-quinoline, N<sup>a</sup>-(7- the group consisting of 7-chloro-4-(amino-1-methyl-butylamino)-quinoline, chloro-4-quinolinyl)-1,4-pentanediamine, 8-(4-amino-1-methylbutylamino)-6-methoxyquinoline (primaquine), N<sup>a</sup>-(6-methoxy-8-quinolinyl)-1,4-pentanediamine, histidine and pyridines selected from the group consisting of nicotinic acid and quinolenic acid and pterines.

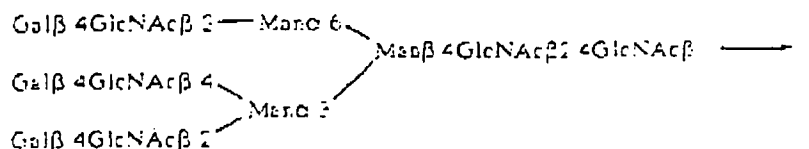
Claim 3. (previously presented) The complex of claim 1 wherein the free  $\text{NH}_3^+$  groups of the polylysine are substituted with a non-charged gluconyl residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex.

Claim 4. (previously presented) The complex of claim 1 wherein recognition-signal is a peptide chosen from the group consisting of

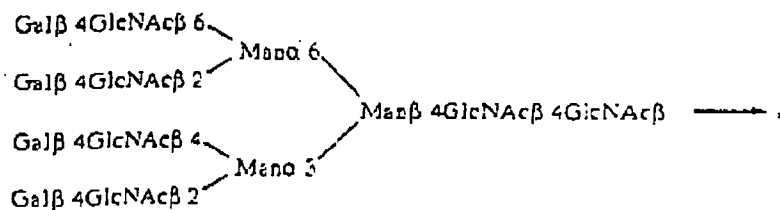
- (a) anti-inflammatory peptides recognized by receptors of the vascular wall,
- (b) ligand peptide of integrins,
- (c) chemiotactic factors and
- (d) peptides hormones.

Claim 5. (previously presented) The complex of claim 1 wherein:  
the monosaccharide are selected from the group consisting of galactose, mannose, fucose,  
glucose, ribose, xylose and rhamnose and  
the complex osides are selected from the group consisting of

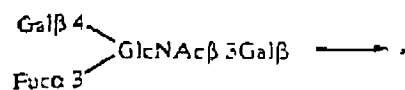
- (a) Asialo-oligoside of the type of iniantenna: lactosamine of



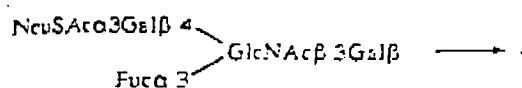
(b) Asialo-oligoside of the type of tetraantennar lactosamin of the formula



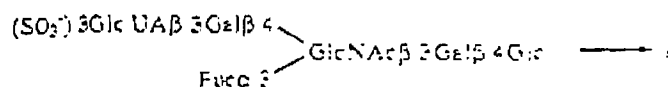
(c) Lewis x of the formula



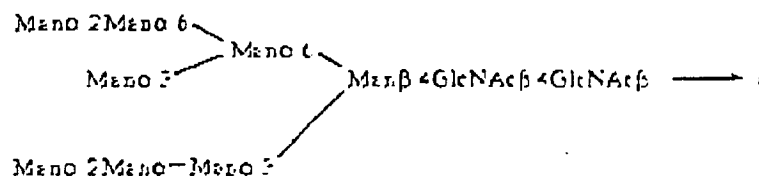
(d) Lewis x sialyl of the formula



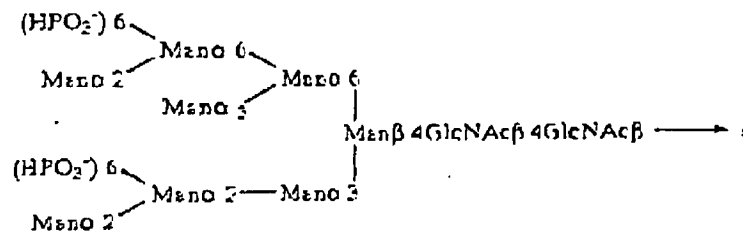
(e) Sulphated Lewis x derivative (HNK1) of the formula



(f) Oligomannoside of the formula

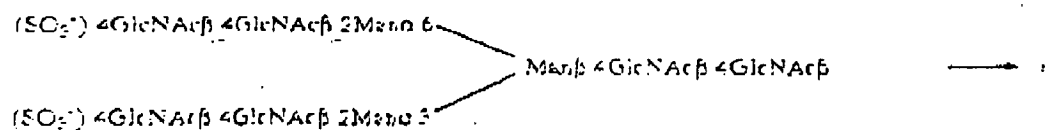


(g) Phosphorylated oligomannoside



50

(h) Oligosaccharide of the type of sulphated lactosamine of the formula



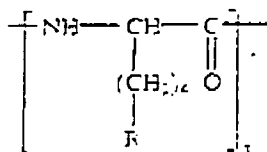
66.

- j. Lactose,
- j. Fucosylated (fucose) GlcNAc $\beta$ Gal $\beta$ Glc,
- k. Fucose (Gal $\beta$ ) GlcNAc $\beta$ Gal $\beta$  and
- l. Mannose-6-phosphate.

Claim 6. (previously presented) The complex of claim 5 wherein the peptides are selected from the group consisting of  
vasodilar intestinal polypeptide (VIP)

HSDAVFTDNYTRLRKQMAVKKYLNSILN-NH<sub>2</sub> (SEQ ID No: 2)  
 atrial natriuretic polypeptide (ANP)  
 SLRRSSCFGGRRMDRIGAOSGLGCNSFRY (SEQ ID No: 3)  
 lipocortin  
 HDMNKVLDL (SEQ ID No: 4)  
 bradykinin  
 RPPGFSPER (SEQ ID No: 5);  
 peptides of integrins, peptide hormones and chemotactics factors.

Claim 7. (previously presented) The complex of claim 1 wherein the polymeric conjugate has the formula:



wherein

p is an integer from 15 to 900;

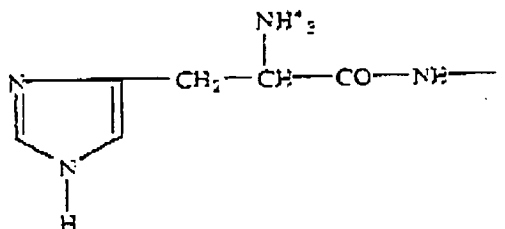
10 to 45% of the radical R being a residue with an imidazole nucleus;

10 to 90% of R being free NH<sub>2</sub> groups;

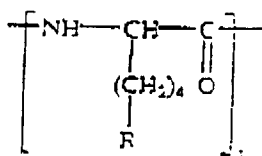
and optionally 0 to 45% of R being -NH-CO-(CHOH)<sub>m</sub>-R<sub>1</sub>, m is an integer from 1

to 15, and R<sub>1</sub> is hydrogen or alkyl of 1 to 15 carbon atoms.

Claim 8. (previously presented) The complex of claim 7 wherein R is a residue with an imidazole nucleus of the formula:



Claim 9. (previously presented) The complex of claim 7 wherein the polymeric conjugate has the following formula:

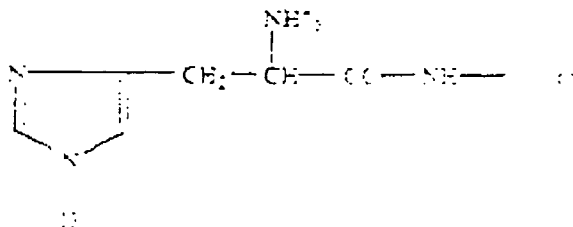


wherein

p is an integer from 15 to 900,

10% to 45% of R is a residue having an imidazole nucleus and optionally a free

$\text{NH}_4^+$ . R has the formula:



with the proviso that all the free  $\text{NH}_2^+$  functions make up at least 50% of the number of monomer units of the polymeric skeleton of the above mentioned polymeric conjugate.

Claim 10. (previously presented) A complex according to claim 1 wherein the nucleic acid is selected from the group consisting of:

- a) marker genes and
- b) genes encoding a therapeutic protein.

Claim 11. (previously presented) Positively charged polymeric conjugate containing a polylysine formed from monomers having free  $\text{NH}_2^+$  groups:

at least 10% of the free  $\text{NH}_2^+$  groups of the said polylysine are substituted by residues which are protonated in a weakly acid medium causing destabilization of cell membranes,

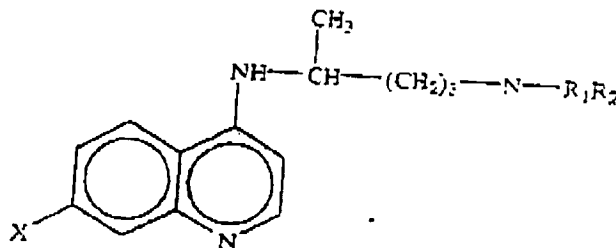
and optionally some of the free  $\text{NH}_2^+$  groups of the said polylysine can be substituted by a molecular with a recognition signal recognized by a cell membrane receptor.

with the proviso that all the free  $\text{NH}_2^+$  groups of the said polylysine make up at least 50% of the number of monomers of the skeleton of the polymeric conjugate.



wherein said residues causing destabilization of cell membranes in a weakly acid

medium ~~belong~~; are selected from the group consisting of family of compounds having an imidazole nucleus, pterines, pyridines and to the family of quinolines of the formula



in which  $R_1$  is hydrogen,  $R_2$  is  $(CH_2)_n-CO_2-H$ ,  $X$  is hydrogen or chlorine and  $n$  is

an integer from 1 to 10, wherein said recognition signal is selected from the group consisting of:

simple osides selected from the group consisting of  $\alpha$  or  $\beta$  conformers of 2-deoxy, of 2-amino or of 2-deoxy, 2-acetamido neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of glycuronic acid derivatives of neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of L-iduronic acid, of keto-deoxy-octonic acid, of M-acetyl-neuraminic acid, or of N-glycoloyl-neuraminic acid; and  $\alpha$  or  $\beta$  conformers of neutral 6-deoxy monosaccharides;

a disaccharide selected from the group consisting of lactose and mannopyranosyl- $\alpha$ -mannopyranose.

and a complex osides selected from the group consisting of Lewis<sup>x</sup>, Lewis<sup>y</sup>, Lewis<sup>z</sup>, oligomannosides and oligolactosamines, and peptides.

Claim 12. (previously presented) The positively charged polymeric conjugate according to claim 11 wherein the free  $\text{NH}_3^+$  groups of the polylysine are substituted with a non-charged residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex, said non-charged residue being a gluconyl.

Claim 13. (previously presented) The composition comprising the complex of claim 1 and an inert pharmaceutical carrier.

Claim 14. (previously presented) A method of transfecting cultured cells comprising incubating said cells in the presence of the composition of claim 13 under conditions wherein said composition enter said cells, and the nucleic acid comprised in the complex of said composition is released to transfect cultured cells.

Claim 15. (previously presented) The method of claim 14 wherein the cells are selected from the group consisting of

cells of hematopoietic strains;

dendritic cells;

liver cells;

skeletal muscle cells;

skin cells;

fibroblasts;

keratinocytes;

adipogenic cells;

melanocytes;

cells of the vascular walls

endothelial;

smooth muscle

epithelial cells of the respiratory tract;

cells of the central nervous system;

cancerous cells; and

cells of the immune system.

Claim 16. (previously presented) The complex of claim 1 wherein the residue causing destabilization of cell membrane in a weakly acid medium is alkylimidazole of 1 to alkyl carbon atoms.